

## **DETAILED ACTION**

Applicant's arguments, filed 4/12/2011, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objects are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

### ***Response to Arguments***

#### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1-7 and 10-16 under 35 U.S.C. 102(b) as being anticipated by WO 01/09198 (WO '198) is maintained.

Applicant argues that the values in Table 3 of WO '193 are inaccurate, and as Table 3 is based on Example 7, the mole ratios of Table 3 should be 100/0; 95/5; 90/10; 80/20; 65/35; and 50/50. Since a polymer that contains even 50% of hydrophobically modified hydroxyalkyl(meth)acrylamide does not dissolve in water, it cannot have the feature required by the claimed invention, that is, having a lower critical solution temperature that changes during incubation in an aqueous solution or medium.

The Applicant's arguments have been fully considered but are not found persuasive. Table 3 of WO '198 compares polymers of Example 6 to Example 7, Example 7 being the control. Example 7 is represented in the columns labeled "NIPAAm/NPMAM" and "NIPAAm/NPMAM (after the hydrolysis treatment).", and have a mol/mol ratio of 0/100 NIPAAm/NPMAM, 5/95 NIPAAm/NPMAM, 10/90 NIPAAm/NPMAM, 20/80 NIPAAm/NPMAM, 35/65 NIPAAm/NPMAM, 50/50 NIPAAm/NPMAM. These ratios are consistent the ratios disclosed in Example 7. Example 6 is represented in the columns labeled "NIPAAm/HPMAM-lactate" and "NIPAAm/HPMAM-lactate (after hydrolysis)", and have a mol/mol ratio of 0/100 NIPAAm/HPMAM-lactate, 5/95 NIPAAm/HPMAM-lactate, 10/90 NIPAAm/HPMAM-lactate, 20/80 NIPAAm/HPMAM-lactate, 35/65 NIPAAm/HPMAM-lactate, and 50/50 NIPAAm/HPMAM-lactate, or in other words, the polymers comprise 100% HPMAM-lactate, 95% HPMAM-lactate, 90% HPMAM-lactate, 80% HPMAM-lactate, 65% HPMAM-lactate, and 50% HPMAM-lactate. Thus, all the polymers of Example 6 have above 50% HPMAM-lactate, i.e. above 50 mol% hydrophobically modified hydroxyalkyl(meth)acrylamide. Regarding Applicant's argument that the polymers of WO '198 cannot have a lower critical solution temperature that changes during incubation in an aqueous solution or medium, WO '198 explicitly teaches that its polymers have a lower critical solution temperature that changes during incubation in an aqueous solution (abstract; claim 1). Thus the Examiner maintains that the polymers of WO '198 polymers do exhibit a lower critical solution temperature that changes during incubation in an aqueous solution, and are homopolymers of a hydrophobically modified

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hydroxyalkyl(meth)acrylamide, or are interpolymers of a hydrophobically modified hydroxyalkyl(meth)acrylamide and up to 50 mole% of acrylamides (In Example 6, the comonomer is an acrylamide).

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The rejection of claims 1-7, 10-13, and 15 under 35 U.S.C. 103(a) as being unpatentable over Neradovic et al (Neradovic et al, *Macromolecules*) is maintained.

The rejection of claims 1-7 and 10-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neradovic et al (*Macromolecules*, 2001) in view of US 5,939,453 ('453) is maintained.

Applicant argues that the NIPAAm/N-(2-hydroxypropyl)methacrylamide lactate copolymers of Neradovic are always at least 50% NIPAAm as shown in Table 1 of Neradovic.

Applicant's arguments have been fully considered but are not found persuasive. The Examiner agrees that in Table 1, the amount of HPMAm-lactate is 50%, 35%, 20%, and 10%. As a first matter, 50 mol% HPMAm-lactate reads on the instant claims which allow 50 mol% HPMAm-lactate (the hydrophobically modified hydroxyalkyl(meth)acrylamide and 50 mol% comonomer. For this reason alone,

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Applicant's arguments are not persuasive. Secondly, the mole% of HPMAm-lactate is a result effective parameter, and it would have been obvious to optimize this mole% to find the optimum balance of hydrophilic/hydrophobic character of the polymer to optimize its role as micelles for drug delivery. Polymeric micelles that are too hydrophilic or hydrophobic will not be effective drug carriers and could allow poorly soluble drug to precipitate (see Neradovic, Introduction). Thus it would have been obvious to find values higher than 50 mol% HPMAm-lactate, through routine experimentation, to adjust the hydrophilic/hydrophobic character of the polymer micelle. The Examiner reiterates that the argument regarding optimization is secondary to the fact that Neradovic explicitly discloses a 50 mol% HPMAm-lactate polymer, which reads on the instant claims, which allow the polymer to be 50 mol% hydrophobically modified hydroxylalkyl(meth)acrylamide.

### ***New Grounds of Rejection***

#### ***Claim Rejections - 35 USC § 112, Written Description***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 24 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

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possession of the claimed invention. The range “wherein the mol % of (a) is in (a) + (b) is 0.1%-99%” is not supported by the application. While the range of 1%-50% in claim 25 is supported at paragraph 93, nowhere in paragraph 93 nor the rest of the specification or original claims is the range “0.1%-99%” contemplated. This range is not explicitly stated in the specification or original claims nor is it implicitly supported by a representative number of examples. For these reasons, the skilled artisan would not accept that applicant had possession of “wherein the mol % of (a) is in (a) + (b) is 0.1%-99%” at the time of filing.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17, 19, and 22-23 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 01/09198 (WO ‘198; document already in record). WO ‘198 discloses a temperature sensitive polymer having a lower critical solution temperature that changes during incubation in an aqueous solution or medium, which polymer is homopolymer of hydroxylpropyl methacrylamide (oligo)lactate (abstract; page 8, line 24 to page 10, line 7; examples; claims 1-20), or a interpolymers of hydroxypropyl methacrylamide (oligo)lactate comprising up to 50% hydroxypropyl methacrylamide (oligo)lactate and an acrylamide (Example 6; Table 3). Such polymers comprise

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hydrophobically modified hydroxyalkyl(meth)acrylamide wherein the hydrophobic group ((oligo)lactate) is bound through an ester bond (a hydrolysable bond). This satisfies instant claim 17. Since the polymers change the LCST during incubation (abstract; page 15, lines 10-14), they are used as controlled release systems and targeting drug compositions, the targeting drug composition may further comprise a homing device. The controlled release system may be in the form of a polymeric micelle in which polyethylene glycol is a hydrophilic block (claim 10), which satisfies instant claim 19. The targeting drug composition may have an average diameter of less than 100 nm (claim 11), which satisfies instant claim 22, and preferably greater than 10 nm and less than 100 nm (page 9, lines 27-31), which satisfies instant claim 23.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neradovic et al (Neradovic et al, *Macromolecules*, 2001) in view of US 5939453 ('453). Neradovic discloses a NIPPAAm/ N-(2-hydroxypropyl)methacrylamide lactate copolymer and micelles made from AB block copolymer containing a polyethylene glycol block and a NIPPAAm/ N-(2-hydroxypropyl)methacrylamide lactate block (page

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7590, tables). The polyethylene glycol block satisfies instant claims 20-21. The N-(2-hydroxypropyl)methacrylamide lactate may comprise 50 mol% of the polymer (Table 1).

Neradovic et al fails to teach an ABA block copolymer as required by instant claim 14, from which claims 20-21 depend.

'453 teaches that AB and ABA block copolymers are equivalents in the art of forming polymer micelles (abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the polymer of Neradovic as an ABA triblock copolymer rather than as an AB diblock. The rationale for this is that the two polymer architectures are recognized as equivalent in the art, and as such are considered to be obvious variants. Therefore the artisan would have a reasonable expectation of success at making the ABA copolymer, and would expect the ABA copolymer to have similar properties to the AB copolymer.

### ***Allowable Subject Matter***

Claims 8, 18 and 25 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL DICKINSON whose telephone number is (571)270-3499. The examiner can normally be reached on Mon-Thurs 9:00am-6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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